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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/731,457 | 12/06/2000 | Ian Popoff | RTS-0182 | 1220 |

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| EXAMINER | |
|---|---|
| SCHULTZ, JAMES | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1635 | |

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 09/731,457 | POPOFF ET AL. | |
| | Examiner | Art Unit | |
| | J. Douglas Schultz | 1635 | |

*-- The MAILING DATE of this communication appears on the cov r sheet with the correspondenc address --*

**Period for R ply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10/2/2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2,4-10 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-10 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Status of Application/Amendment/Claims*

Applicant's response filed October 2, 2003 has been considered. Rejections and/or objections not reiterated from the previous office action mailed July 16, 2003 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Response to Arguments*

Claims l, 2, 4-10, and 12-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dualan et al., in view of Taylor et al., Baracchini et al, Hayes et al and Krishnamoorthy et al., for the same reasons of record as set forth in the Office action dated July 16, 2003.

Applicants have amended the claims to read on antisense targeted to human DDB1, and further claim that such antisense must be able to inhibit said DDB1 by at least 60%. These claim limitations are not sufficient to clear the claims from the instant rejection, because Taylor et al. teach that only 3-6 sequences need to be screened in order to find one that inhibits 66-95% *in vitro*. Taylor et al. thus teaches that one of ordinary skill in the art, using art recognized methods, would have an expectation of success in finding compounds that inhibit at least 60%. Furthermore, applicants limitation that DDB1 is of human origin does not free the claim from the rejection, because Dualan continue to teach the same human DDB1 mRNA transcript that applicants' claim as a target.

Applicants assert that the Office action is mistaken in its conclusion that it would have been obvious to one of ordinary skill in the art to make and use antisense targeted to DDB1 as instantly claimed. In brief review, it was set forth in the previous Office action that, because Dualan teach the cDNA sequence of the instantly claimed target, and because Hayes and Krishnamoorthy teach motivation for inhibiting said target, and finally because Taylor et al. and Baracchini et al. teach methods of making and using antisense molecules to inhibit targets of known sequence, that this combination teaches all the requisite elements and provides the motivation and expectation of success to render applicants claimed invention obvious.

Applicants' response alleges that the examiner is mistaken because if this were true, then the ultimate conclusion would be that "all oligonucleotides that inhibit expression of [a known] gene are obvious." Applicants contend that "the mere fact that the Taylor reference reports that antisense oligonucleotides that inhibit expression of a particular gene can be designed does not render all subsequent antisense oligonucleotide compounds of a known gene sequence." Applicants further argue that "[i]ndeed, the Examiner's ultimate conclusion would require Applicants to either: 1) develop new methods of obtaining antisense oligonucleotides, in which case Applicants may be able to obtain product-by-process claims or method claims, or 2) develop antisense oligonucleotides to previously unknown gene sequences. In either case, all novel antisense oligonucleotides targeted to a known gene sequence would be deemed obvious in view of the current reasoning set forth in the Office Action." Applicants thus conclude that in regards to the instant rejection of obviousness, "this reasoning...is deficient".

In response, it is noted that applicants have apparently not disputed that the instant rejection met the proper criteria in showing that the elements are taught and that motivation

exists in determining that the claimed invention is obvious. That is, applicants have not argued that motivation is lacking, or that the instant combination of references fails to teach all the elements of the claimed invention. Although applicants assert later in their response that the examiner has not established an expectation of success emanating from this combination of references, an assertion that is not considered convincing as explained below, applicants have not pointed to any deficiency or error in motivation or element.

Applicants primary assertion is that the "ultimate conclusion" of the examiner's obviousness analysis serves to render all novel antisense oligonucleotides targeted to a known gene sequence obvious. However, this is not agreed with. Applicants have not claimed any particular novel compound, but rather, have claimed the entire genus of compounds that inhibits DDB1. Applicants are directed to the claim language, which is drawn to any "compound 8 to 50 nucleobases in length targeted to a 5' untranslated region, a start codon region, a coding region, a stop codon region, or a 3' untranslated region of a nucleic acid molecule encoding human Damage specific DNA binding protein 1, p127 of SEQ ID NO: 3, wherein said compound inhibits the expression of human Damage specific DNA binding protein 1, p127 by at least 60%". Regarding applicants' arguments that they would have to develop new methods of obtaining antisense or identify novel targets are not considered germane to the analysis of obviousness, since the prior art teaches all the elements, and the motivation, and the expectation of success of applicants claimed invention. As a point of interest, applicants list of means by which an antisense patent may be obtained in the instant application is by no means exhaustive, and furthermore, does not speak to whether the claimed invention is novel, or obvious, or properly described for purposes of 35 U.S.C. § 112 first paragraph.

No reasoning has ever been presented in any Office action that renders any specific antisense compound obvious, because none has ever been claimed. Rather, applicants claims drawn to the broad genus of any compound that inhibits DDB1 is considered obvious for reasons of record. Since applicants have not presented any arguments pertaining to whether the references teach the elements or motivation as they relate to said genus, and since applicants are arguing the unobviousness of specific sequences that haven't actually been claimed, such arguments are not considered persuasive.

Applicants allege that the combination of references does not provide a reasonable expectation of success, and that the instant references rise only to the level of an improper "obvious to try" standard. This is not adopted, because, as pointed out in the previous Office action, the Taylor reference teaches that the antisense-mediated inhibition of known sequence *in vitro* is routine to one of ordinary skill in the art. Taylor teaches that "only 3-6 sequences need to be screened in order to find one that inhibits 66-95% *in vitro*. While applicants argue that such teachings as those found in Taylor are general, and don't provide specific direction, it is maintained that Taylor indicates that a specific blueprint such that one of ordinary skill could design and screen for active molecules would be easily available to one of ordinary skill. Furthermore, applicants are directed to the teachings of Baracchini, who provide explicit detailied directions on how to design and screen molecules for specific levels of inhibitory activity, complete with precise protocols of how to make and use antisense oligos to inhibit a gene of known sequence, including materials related to synthesis of such oligos *de novo*, and also include individual manufacturers of starting reagents, incubation times, concentrations, cell

types, and assays for inhibitory capability. Baracchini clearly teaches one of ordinary skill how to screen for inhibitory compounds.

While Taylor indicates a high level of success may be expected by one of ordinary skill without providing voluminous detail, the teachings of Baracchini clearly make up for this. Furthermore, nowhere does Taylor indicate that success *in vitro* is speculative, or rises only to the level of "obvious to try". This is evidenced by applicants' own words, at the last sentence of page 5: "the Taylor reference supports the enablement of antisense technology". The examiner agrees, to the extent that such teachings are confined to *in vitro* results.

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 703-308-9355. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

James Douglas Schultz, PhD